Cross-sectional studies

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Concepts to take home

• Principle & types of cross-sectional study designs
• Advantages & disadvantages
• Prevalence, prevalence ratio, prevalence odds ratio
• Bias in cross-sectional studies
• Usefulness of cross-sectional studies
Principle of cross-sectional studies

- Conducted at a single point in time or over a short period of time (snapshot of population)
- Exposure status and disease status are measured at one point in time or over a period.
- Can be either descriptive or analytic, depend on design
  - Prevalence studies (descriptive cross-sectional study)
  - Comparison of prevalence among exposed and non-exposure (analytic cross-sectional study)
Analytic Cross-sectional Study

* Comparative groups
* One measurement, no follow up
* Association?

snapshot of population

Analytic Cross-sectional Study

exercise

Obesity

<table>
<thead>
<tr>
<th></th>
<th>O+</th>
<th>O-</th>
</tr>
</thead>
<tbody>
<tr>
<td>ex+</td>
<td>50</td>
<td>100</td>
</tr>
<tr>
<td>ex-</td>
<td>20</td>
<td>80</td>
</tr>
</tbody>
</table>

Relative prevalence O+ = (50/150)/(20/100) = 1.67

Association, no sequence
Types of cross-sectional studies

- Descriptive cross-sectional study
- Analytic cross-sectional study
- Repeated cross-sectional study

Cross-sectional studies

- **Descriptive**
  - Collected number of cases and number of total population.
  - Can assess only prevalence of disease or other health events, also called “prevalence study”.

- **Analytic**
  - Expose and disease status are assessed simultaneously.
  - Can determine association between exposure and disease.
Descriptive cross-sectional study

- Measures prevalence of disease at a single point in time or over a short period of time. Two types:
  - Point prevalence: *Do you currently use a NSAIDS?*
  - Period prevalence: *Have you used a NSAIDS in the past 6 months?*

Analytic cross-sectional study

- Measure association between expose and outcome.
  - Expose and outcome are assessed simultaneously.
  - Measure of association;
    - Prevalence ratio
    - Prevalence odds ratio
Cross-sectional Study Design

- Exposed have disease (A)
- Exposed do not have disease (B)
- Non-exposed have disease (C)
- Non-exposed do not have disease (D)

Population

Sample

2 x 2 tables

<table>
<thead>
<tr>
<th>Disease</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td>No</td>
<td>C</td>
<td>D</td>
</tr>
</tbody>
</table>

Risk Factor

- Yes
- No

A+B
C+D
A+C
B+D
Measure of prevalence

\[
\text{prevalence} = \frac{A+C}{A+B+C+D}
\]

Prevalence of disease among exposure

\[
= \frac{A}{A+B}
\]

Prevalence of disease among non-exposure

\[
= \frac{C}{C+D}
\]

Measure of association

1. Prevalence ratio

\[
= \frac{\text{Prevalence of disease among exposure}}{\text{Prevalence of disease among non-exposure}}
\]

\[
= \frac{A}{A+B} / \frac{C}{C+D}
\]
Measure of association

2. Prevalence odds ratio

- Odds of exposure among cases
  \[ \frac{\text{exposed cases}}{\text{all cases}} / \frac{\text{unexposed cases}}{\text{all cases}} = \frac{A}{A+C} / \frac{C}{A+C} = \frac{A}{C} \]

- Odds of exposure among non-cases
  \[ \frac{\text{exposed non-cases}}{\text{all non-cases}} / \frac{\text{unexposed non-case}}{\text{all non-cases}} = \frac{B}{B+D} / \frac{D}{B+D} = \frac{B}{D} \]

Prevalence odds ratio (OR) = \( \frac{\text{Odds of exposure among cases}}{\text{Odds of exposure among non-cases}} = \frac{AD}{BC} \)

Example: Medical exam & X-rays to diagnose osteoarthritis of the knee

<table>
<thead>
<tr>
<th>Disease</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk Factor</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>A</td>
<td>B</td>
<td>C</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Osteoarthritis</th>
<th>yes</th>
<th>no</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity yes</td>
<td>80</td>
<td>20</td>
</tr>
<tr>
<td>no</td>
<td>40</td>
<td>60</td>
</tr>
</tbody>
</table>
Prevalence ratio

prevalence of osteoarthritis: 120/200 = 0.6

Prevalence of osteoarthritis among obese subjects: 80/100 = 0.8

Prevalence of osteoarthritis among non-obese subjects: 40/100 = 0.4

Prevalence ratio = 0.8/0.4 = 2.0

Interpretation: the proportion of people with OA is 2-fold greater if a person is obesity

Prevalence odds ratio

Prevalence odds ratio

= \frac{80 \times 60}{20 \times 40} = 6.0

Interpretation:
The odds that OA patients would be obesity appear to be about 6 times the odds that non-OA patients would be obesity.
The estimated OA diagnosis among the obese subjects is 6.0 times greater than that among the non-obese.
Repeated cross-sectional study

- Exposure and disease are determined at baseline and reassessed throughout a period of follow-up.

- Distinction between repeated cross-sectional study & longitudinal, prospective cohort

### Repeated cross-sectional data

<table>
<thead>
<tr>
<th>AGE (yr)</th>
<th>1985</th>
<th>1990</th>
<th>1995 Year</th>
<th>2000</th>
<th>2005</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>A</td>
<td>B</td>
<td>C</td>
<td>D</td>
<td>E</td>
</tr>
<tr>
<td>35</td>
<td>B</td>
<td>C</td>
<td>D</td>
<td>E</td>
<td>F</td>
</tr>
<tr>
<td>30</td>
<td>C</td>
<td>D</td>
<td>E</td>
<td>F</td>
<td>G</td>
</tr>
<tr>
<td>25</td>
<td>D</td>
<td>E</td>
<td>F</td>
<td>G</td>
<td>H</td>
</tr>
<tr>
<td>20</td>
<td>E</td>
<td>F</td>
<td>G</td>
<td>H</td>
<td>I</td>
</tr>
</tbody>
</table>
Longitudinal or cohort data

<table>
<thead>
<tr>
<th>AGE (yr)</th>
<th>40</th>
<th>35</th>
<th>30</th>
<th>25</th>
<th>20</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A</td>
<td>B</td>
<td>C</td>
<td>D</td>
<td>E</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>C</td>
<td>D</td>
<td>E</td>
<td>F</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>D</td>
<td>E</td>
<td>F</td>
<td>G</td>
</tr>
<tr>
<td></td>
<td>D</td>
<td>E</td>
<td>F</td>
<td>G</td>
<td>H</td>
</tr>
<tr>
<td></td>
<td>E</td>
<td>F</td>
<td>G</td>
<td>H</td>
<td>I</td>
</tr>
</tbody>
</table>

| Year     | 1985 | 1990 | 1995 Year | 2000 | 2005 |

Advantages of cross-sectional studies

- Good for describing the magnitude and distribution of health problems.
- Generalizable results if population based sample
- Quick, conducted over short period of time, easy, inexpensive.
- Can study multiple exposures and disease outcomes simultaneously.
Disadvantages of cross-sectional studies

- Cannot establish sequence of events
  - Not for causation or prognosis
- Impractical for rare diseases if pop based sample (eg, gastric CA 1/10,000).
- Possible bias since only survivors are available for study

Cross-sectional study design

Survival time

Hypothetical cohort

Time of the study

Time
Bias in Cross-Sectional Studies

1. Selection bias
   - Sampling bias: representativeness
   - Prevalence-incidence bias (Neyman bias)
   - Response and non-response bias

2. Measurement bias
   - Misclassified (misdiagnosed, undiagnosed)
     - Recall bias
     - Lead-time bias
     - Length biased sampling

3. Confounding

Sampling in Epidemiology

- Definitions
  - **Sampling unit** – the basic unit around which a sampling procedure is planned
    - Person
    - Group – household, school, district, etc.
    - Component – eye, physiological response
  - **Sampling frame** – list of all of the sampling units in a population
  - **Sample** – collection of sampling units from the eligible population
Sampling in Epidemiology

- **Probability Sample**
  - Simple random sample
  - Stratified random sample
  - Cluster sample
  - Multistage sample
  - Systematic sample

- **Non-probability Sample**
  - Convenience sample
  - Consecutive sample
  - Quota sample
  - Volunteer sample

**PROBABILITY SAMPLE**
Sampling in Epidemiology

- Simple random sampling
  - Each sampling unit has an equal chance of being included in the sample
  - In epidemiology, sampling generally done without replacement as this approach allows for a wider coverage of sampling units, and as a result smaller standard errors

Example of simple, random sampling

Numbers are selected at random
Stratified random sample

- The sampling frame comprises groups, or strata, with certain characteristics
- A sample of units are selected from each group or stratum

Stratified Random selection for drug trail in hypertension
Sampling in Epidemiology

- Cluster sampling
  - Clusters of sampling units are first selected randomly
  - Individual sampling units are then selected from within each cluster

Sampling in Epidemiology

- Multistage sampling
- Similar to cluster sampling except that there are two sampling events, instead of one
  - Primary units are randomly selected
  - Individual units within primary units randomly selected for measurement
Sampling in Epidemiology

- Systematic sampling
  - The sampling units are spaced regularly throughout the sampling frame, e.g., every 3\textsuperscript{rd} unit would be selected

  - May be used as either probability sample or not
    - Not a probability sample unless the starting point is randomly selected
    - Non-random sample if the starting point is determined by some other mechanism than chance
NON-PROBABILITY SAMPLE

Sampling in Epidemiology

- Convenience sample
  - Case series of patients with a particular condition at a certain hospital
  - “Normal” graduate students walking down the hall are asked to donate blood for a study
  - Children with febrile seizures reporting to an emergency room

Investigator decides who is enrolled in a study
Sampling in Epidemiology

- **Consecutive sample**
  - A case series of *consecutive* patients with a condition of interest
  - Consecutive series means ALL patients with the condition within hospital or clinic, not just the patients the investigators happen to know about

- **Advantages**
  - Removes investigator from deciding who enters a study
  - Requires protocol with definitions of condition of interest
  - Straightforward way to enroll subjects

- **Disadvantage**
  - Non-random

**Quota sampling:** selecting fixed numbers of units in each of a number of categories.
Prevalence-incidence bias (Neyman bias)

- It arises when a gap in time occurs between exposure and selection of study subjects.

Neyman bias example

- The study of myocardial infarction and snow shovelling (the exposure of interest) would miss individuals who died in their driveways and thus never reached a hospital.
- This eventuality might greatly lower the association of infarction associated with this strenuous activity.
Prevalence-incidence bias (Neyman bias)

Framingham study

<table>
<thead>
<tr>
<th></th>
<th>Incidence</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Developed CHD by exam 6</td>
<td>Did not develop CHD by exam 6</td>
</tr>
<tr>
<td>High serum cholesterol</td>
<td>85</td>
<td>462</td>
</tr>
<tr>
<td>Low serum cholesterol</td>
<td>116</td>
<td>1511</td>
</tr>
<tr>
<td></td>
<td>201</td>
<td>1973</td>
</tr>
<tr>
<td>ORs</td>
<td>2.40</td>
<td></td>
</tr>
</tbody>
</table>

Friedman et al. Amer J Epid 1966;83:366

Lead-time bias

Lung cancer-specific survival is measured from the time of diagnosis (Dx) of lung cancer to the time of death.

If a lung cancer is screen-detected before symptoms (Sx), then the lead time in diagnosis equals the length of time between screening detection and when the first signs/symptoms would have appeared.

Even if early treatment had no benefit, the survival of screened persons would be longer simply by the addition of the lead time.
**Length biased sampling**

- **Length biased sampling**: diseases that have long duration will over-represent the magnitude of illness while short duration will under-represent illness.

**Length bias**

- The cancers that grow slowly are easier to detect because they have a longer pre-symptomatic period of time when they are detectable.
- Thus, the screening test detects more slowly growing cancers.
Usefulness of cross-sectional study design

- Diagnostic test
- Prevalence study
  - Describe distribution of variables
  - Health care services
- Examine associations among variables
  - Hypothesis generating for causal links
- Prediction score

Accuracy of a Test Result

<table>
<thead>
<tr>
<th>Test</th>
<th>Disease</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>True positive</td>
<td>a</td>
<td>b</td>
</tr>
<tr>
<td></td>
<td>False positive</td>
<td>c</td>
<td>d</td>
</tr>
<tr>
<td>Negative</td>
<td>False negative</td>
<td>c</td>
<td>d</td>
</tr>
<tr>
<td></td>
<td>True negative</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Sensitivity = true positive rate = a / a + c
Specificity = true negative rate = d / b + d
# Accuracy of a Test Result

<table>
<thead>
<tr>
<th>Term</th>
<th>General Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>Proportion of those with the condition who have a positive test</td>
</tr>
<tr>
<td>Specificity</td>
<td>Proportion of those without the condition who have a negative test</td>
</tr>
<tr>
<td>Accuracy</td>
<td>Proportion of accurate diagnostic test</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>Proportion of those with a positive test who have the condition</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>Proportion of those with a negative test who do not have the condition</td>
</tr>
</tbody>
</table>

## Example Calculation

<table>
<thead>
<tr>
<th>Term</th>
<th>Example</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>$a/(a+c)$</td>
<td>$80/100 (80%)$</td>
</tr>
<tr>
<td>Specificity</td>
<td>$b/(b+d)$</td>
<td>$90/100 (90%)$</td>
</tr>
<tr>
<td>Accuracy</td>
<td>$a+d/n$</td>
<td>$170/200 (85%)$</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>$a/(a+b)$</td>
<td>$80/90 (90%)$</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>$d/(c+d)$</td>
<td>$90/110 (82%)$</td>
</tr>
</tbody>
</table>

## Clinical Interpretation

- **Sensitivity**: Is the test detecting true cases of disease?
  - (Ideal is 100%: 100% of cases are detected)

- **Specificity**: Is the test excluding those without disease?
  - (Ideal is 100%: 100% of non-cases are negative)
### Steps of conducting cross-sectional study

<table>
<thead>
<tr>
<th>Questions to ask</th>
<th>Steps to take</th>
<th>Important elements/step</th>
</tr>
</thead>
<tbody>
<tr>
<td>What is the problem and why should it be studied?</td>
<td>Choose the problem and analyze it</td>
<td>• Problem identification &lt;br&gt; • Prioritizing problem &lt;br&gt; • Problem analysis</td>
</tr>
<tr>
<td>What information is already available</td>
<td>Literature review</td>
<td>• Literature and other available information</td>
</tr>
<tr>
<td>What do we hope to achieve?</td>
<td>Formulation of objectives</td>
<td>• General and specific objectives &lt;br&gt; • Hypothesis</td>
</tr>
</tbody>
</table>

### Questions to ask

| What data do we need to meet our objectives? How will this be collected? |
| Who will do? What? and when? |
| How will the study be administered? |

<table>
<thead>
<tr>
<th>Steps to take</th>
<th>Important elements/step</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research methodology</td>
<td>• Sampling &lt;br&gt; • Variables &lt;br&gt; • Data collection techniques &lt;br&gt; • Plan for data collection, processing, and analysis &lt;br&gt; • Ethics, pilot study</td>
</tr>
<tr>
<td>Work plan</td>
<td>• Personal-training &lt;br&gt; • Time table</td>
</tr>
<tr>
<td>Plan for project administration</td>
<td>• Administration and monitoring</td>
</tr>
</tbody>
</table>
Source: Step in design of a cross-sectional study (Modified from Varkevisser et al)

Questions to ask  Steps to take  Important elements/step

What resource do we need?  Resource identification and acquisition  • Money  • Personnel  • Materials, equipment

How will we use the results  Proposal summary, paper, and presentation

Source: Step in design of a cross-sectional study (Modified from Varkevisser et al)

โครงการวิจัย การประเมินความชุกของโรคไตเรื้อรังในประชากรไทย

Screening and Early Evaluation of Kidney Disease
Thai-SEEK project
Prevalence and risk factors of chronic kidney disease in the Thai adult population: Thai SEEK study

Atiporn Insuthit1, Ammarin Thakkinstian1, Amnart Chaiprasert2, Pompun Sanghawan3, Pongsaithorn Gojaysen4, Kriwiporn Kiatissathorn5, Leena Ongsiyoorth6, Somlak Vanavan6, Dhavec Sirivongs1, Prapapim Thirakhup7, Bharati Mittal7, Ajay K. Singh8 and the Thai-SEEK Group

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Correspondence and offprint requests to: Atiporn Insuthit; E-mail: tci@mahidol.ac.th

Primary objective

- To describe the distribution of CKD stages and severity
Methodology

- **Study design**: Cross-sectional study
- **Study period**: August 2007 to January 2009

The study was approved by the IRB of the Faculty of Medicine at Ramathibodi Hospital, Mahidol University

Study subjects

- **Inclusion criteria**
  - Aged 18 or older
  - No menstruation period
  - No fever for at least a week before examination date
  - Willingness to participate and provide a signed consent form
- **Exclusion criteria**
  - Blood or urine specimens were not taken
Stratified-cluster random sampling

Thailand

N  NE  C/E  S  BK

province

Urban

District

Rural

District

Sample size estimation

- Prevalence from previous studies: 3%-13.7%
- Type I error = 0.05
- Design effect = 3
- Calculate 95% CI
  - Sample size 4,000: 95%CI = 11.9-15.7
  - Sample size 3,000: 95%CI = 11.7-16.0
Sample size estimation

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Sample size estimation

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  - Sample size 3,000: 95% CI = 11.7-16.0
## Measurement

- **Serum creatinine:** Standardized with IDMS method
- **Urine albumin:** Immunoturbidimetry
- **Hematuria:** Trained technician at site
Pre-camp training

Camp day
Station 1 Inform consent

Station 2 Registration
Station 3 Blood sample collection

Station 4 Urine sample collection
Station 5 Interview

Station 6 Physical examination
Station 7 Education

Material
Station 8 Check point for completeness

RESULTS
# CKD prevalence in Thai population

**Thai SEEK study**

3,459 general population

Age 45.2 (0.8), Male 45.3%

<table>
<thead>
<tr>
<th>CKD staging</th>
<th>Overall N=3459</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>II</td>
</tr>
<tr>
<td>No*</td>
<td>Prevalence (95%CI)</td>
</tr>
<tr>
<td>134</td>
<td>3.3 (2.3, 4.1)</td>
</tr>
<tr>
<td>8.9 (6.8, 11.0)</td>
<td></td>
</tr>
</tbody>
</table>


---

# Projection of expected numbers of adult population

**Thai SEEK study**

<table>
<thead>
<tr>
<th>Year</th>
<th>Adult Population</th>
<th>Expected CKD cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td>3.9 million</td>
<td>5.6 million</td>
</tr>
<tr>
<td>2009</td>
<td>3.9 million</td>
<td>5.7 million</td>
</tr>
<tr>
<td>2010</td>
<td>4.0 million</td>
<td>5.8 million</td>
</tr>
<tr>
<td>2011</td>
<td>4.8 million</td>
<td>7.0 million</td>
</tr>
<tr>
<td>2012</td>
<td>4.9 million</td>
<td>7.1 million</td>
</tr>
<tr>
<td>2013</td>
<td>5.0 million</td>
<td>7.2 million</td>
</tr>
</tbody>
</table>
Estimation of CKD prevalence according to age and gender

Estimation of CKD prevalence according to region
Risk factors associated with CKD

<table>
<thead>
<tr>
<th>Factors</th>
<th>Stage I-V</th>
<th>No CKD</th>
<th>Adjusted OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, year</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 70</td>
<td>139</td>
<td>128</td>
<td>7.34 (4.18, 12.90)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>60 – 69</td>
<td>148</td>
<td>255</td>
<td>3.63 (2.26, 5.86)</td>
<td>0.001</td>
</tr>
<tr>
<td>40 - 59</td>
<td>237</td>
<td>1,227</td>
<td>1.71 (1.16, 2.52)</td>
<td>0.017</td>
</tr>
<tr>
<td>&lt; 40</td>
<td>102</td>
<td>1,223</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>History of kidney stone</td>
<td>74</td>
<td>95</td>
<td>2.72 (1.80, 4.12)</td>
<td>0.002</td>
</tr>
<tr>
<td>DM</td>
<td>183</td>
<td>251</td>
<td>2.72 (1.57, 4.73)</td>
<td>0.005</td>
</tr>
<tr>
<td>Hypertension</td>
<td>329</td>
<td>626</td>
<td>1.96 (1.44, 2.67)</td>
<td>0.002</td>
</tr>
<tr>
<td>Uric acid, mg/dl</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 5.61</td>
<td>331</td>
<td>938</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>4.40 – 5.61</td>
<td>166</td>
<td>960</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>&lt; 4.40</td>
<td>129</td>
<td>935</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Using traditional medicine</td>
<td>263</td>
<td>880</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>356</td>
<td>1,534</td>
<td>1.70 (1.18, 2.43)</td>
<td>0.013</td>
</tr>
<tr>
<td>Male</td>
<td>270</td>
<td>1,299</td>
<td>1.00</td>
<td></td>
</tr>
</tbody>
</table>

Cross-sectional Design

- Rapid, Easy
- Co-operative
- Inexpensive
- Prevalence study
- First step of cohort
- Cross-sectional association
- Blinded: single
Summary

- Principle & types of cross-sectional study designs
- Advantages & disadvantages
- Prevalence, prevalence ratio, prevalence odds ratio
- Bias in cross-sectional studies
- Usefulness of cross-sectional studies